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APPLICATION NUMBER: *60/529,093*
FILING DATE: *December 15, 2003*

Certified by

Jon W Dudas

Acting Under Secretary of Commerce
for Intellectual Property
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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a **PROVISIONAL APPLICATION FOR PATENT** under 37 CFR 1.53 (b)(2).

Docket Number	27288	Type a plus sign (+) inside this box ->	+

INVENTOR(s) / APPLICANT(s)

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TITLE OF THE INVENTION (280 characters max)

THERAPEUTIC DRUG-ELUTING ENDOLUMINAL COVERING TO PROMOTE VASCULAR REHEALING

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ **Specification**	*Number of Pages*	3	☑ **Applicant is entitled to Small Entity Status**	
☑ **Drawing(s)**	*Number of Sheets*	2	☑ **Other** (specify)	**6 Claims**

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☐ A check or money order is enclosed to cover the filing fees		**FILING FEE AMOUNT ($)**	**$ 80.-**
☑ The Commissioner is hereby authorized to charge filing fees and credit Deposit Account Number:	**50-1407**		

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☑ No

☐ Yes, the name of the US Government agency and the Government contract number are: _____

Respectfully submitted,

SIGNATURE _____ Date December 11, 2003

25,457
REGISTRATION NO. *(if appropriate)*

TYPED or PRINTED NAME **SOL SHEINBEIN**

☐ Additional inventors are being named on separately numbered sheets attached hereto

The PTO did not receive the following listed item(s) Small Entity

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

Therapeutic Drug-Eluting Endoluminal Covering to Promote Vascular Rehealing

Inventors: Dror Seliktar and Rafael Beyar

BACKGROUND

The present invention addresses the clinical need of prevention of restenosis after balloon angioplasty. Balloon angioplasty and stenting have been developed to become the major revascularization methods worldwide for treatment of coronary stenosis. However, one of the limitations of this procedure is the significant renarrowing of the vessel wall, otherwise known as restenosis. Restenosis, which occurs within 6 months in 30-40% of patients, results in an obstructive neointimal layer formed at the injury site post-operatively. Smooth muscle cell (SMC) migration, proliferation, and matrix deposition are putative contributors to intimal thickening and arterial remodeling. Thrombosis has also been implicated as a potential causative factor in restenosis, since thrombus can serve as a cytokine-rich matrix for smooth muscle cell migration and proliferation.

Metallic stents used with balloon angioplasty have contributed to an improved efficacy for this procedure in recent years. It is estimated that almost 80% of contemporary procedures are performed with the use of coronary stents. In certain cases, stents are being modified with antiproliferative agents such as rapamycin, paclitaxel, tranilast, and trapidil in order to minimize intimal thickening by slowing down the SMC response to the balloon injury. Despite the widespread acceptance of stent coatings, this strategy could nevertheless benefit from additional refinement in order to further improve its long-term clinical efficacy. For example, using a stent as a drug delivery carrier limits the effective surface area of delivery to 13% of the entire coronary injury site. In such cases, the stent has to be loaded with a much higher concentration of drug in order to accomplish its specific aim. Higher drug concentrations in turn lead to adverse edge effects at the interface of the stent and the artery wall which could ultimately reduce efficacy of the procedure. Therefore, if balloon angioplasty technologies could simultaneously allow for the physical support of the stent with the pharmacological benefit of a therapeutic paving of the entire injury site, the process of vascular healing following angioplasty can be guided much more effectively. For this reason, we propose using modified material coatings over the injury site to favorably and systematically regulate cellular events following angioplasty.

THE INVENTION

The invention addresses post-traumatic intravascular rehealing associated with minimally invasive balloon angioplasty and stenting. Through the application of a micro-thin biodegradable sheet on the internal margins of an endoluminal vascular injury, site specific administration of cytotherapeutic drugs will promote reendothelialization and prevent thrombosis and vessel restenosis by intimal hyperplasia. The biodegradable sheet can accommodate the site-specific release of both cytotherapeutic drugs and cellular factors according to the determined needs of the vascular repair process. The sheet is designed to be biodegradable such that the during the repair process, the material will eventually give way to subcellular tissue, with the non-toxic degradation products being released into the circulation and cleared from the body. The release of cytotherapeutic drugs, cellular factors, and degradation products are all controlled via the structural parameters of the preformed material, including chemical composition, polymeric chain length, cross-linking density, and hydrophobicity of the material. Degradation and drug delivery parameters can be designed for several days and up to several months, according to the determined needs of the vascular repair process. Furthermore, the material is designed to be non-thrombogenic based on its anti-adhesive characteristics. The material does not support the adsorption of proteins and coagulations factors, including adhesion of platelets and circulation cells. The material will be delivered onto the injury site of the vessel using an intravascular stent (Fig 1). The polymer sheet will be rolled over the stent and temporarily secured in place to allow for safe passage to the local target in the vasculature (Fig 2). At the site of administration, the stent will be expanded with the rolled sheet overtop, causing the thin sheet to unroll and hug the internal margins of the target vessel. The material will stay in place on the artery wall for the duration of its therapeutic function using the stent as an anchoring mechanism (Fig 3).

Claims:

1. A drug eluting sheet essentially as described and exemplified herein.
2. The use of a drug eluting sheet essentially as described and exemplified herein.
3. The use of a drug eluting sheet for promoting vascular rehealing essentially as described and exemplified herein.
4. The use of a drug eluting sheet for preventing restenosis essentially as described and exemplified herein.
5. The use of any of claims 2-4 in context of balloon angioplasty.
6. The use of any of claims 2-4 in context of stenting.

FIGURES

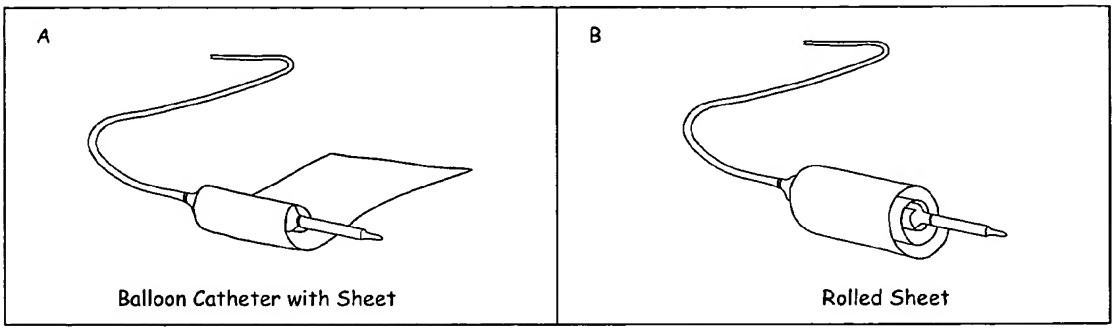

Figure 1: A thin, biodegradable drug-eluting sheet will be rolled overtop a balloon catheter containing a metallic stent (A). Once the sheet is completely rolled over the catheter (B), it is secured in place with a very mild medical grade adhesive.

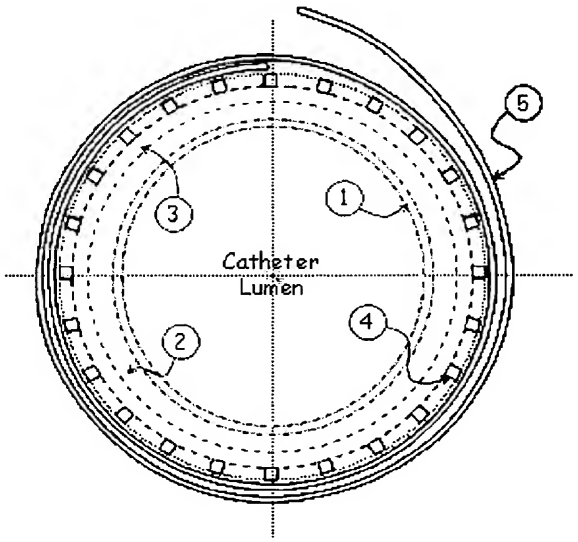

Figure 2: A Schematic illustration of a micro-thin, biodegradable, drug-eluting sheet rolled over a balloon catheter holding a metallic stent. The catheter lumen is proceeded by: (1) the wall of the catheter, (2) the uniflated lumen of the balloon, (3) the wall of the balloon, (4) the stent struts, (5) and the rolled, drug-eluting sheet.

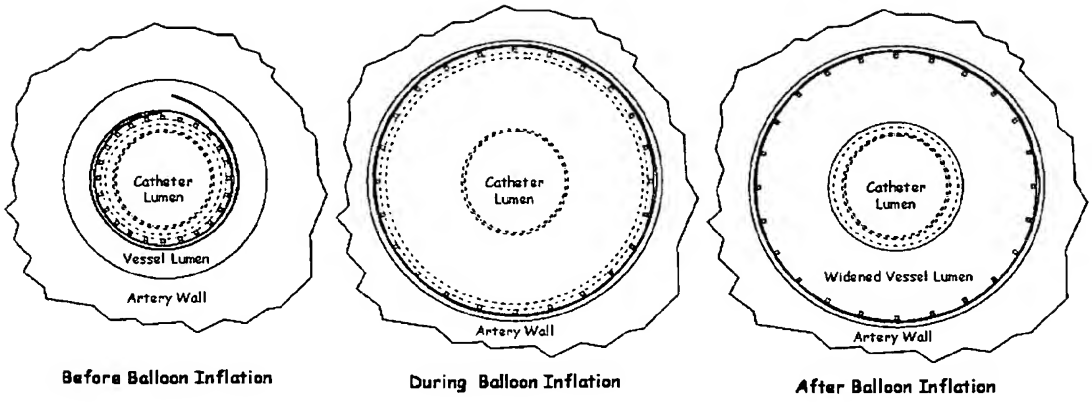

Figure 3: A balloon catheter with a metallic stent and a drug eluting sheet rolled overtop is inflated inside the vessel lumen (left), causing the stent to expand and the drug eluting sheet to unroll onto the artery wall (middle). Following the procedure, the expanded stent fixes the unrolled drug-eluting sheet on the vessel wall.